

WE CLAIM:

1. A method for ejecting a cell from within a fluid near the surface thereof
5 comprising delivering sufficient focused energy to the fluid to eject the cell therefrom,
wherein the ejected cell is contained in a droplet of said fluid.

2. The method of claim 1, wherein said focused energy comprises focused
acoustic energy.

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3. The method of claim 1, wherein said focused energy comprises focused
electromagnetic energy.

4. The method of claim 1, further comprising, prior to delivering said focused
15 energy to the fluid, determining whether the cell is sufficiently close to the surface to
enable ejection of the cell in a droplet of said fluid.

5. The method of claim 1, wherein a substrate is positioned over said fluid with
a surface of the substrate facing the surface of the fluid, such that the cell-containing
20 droplet is ejected onto the substrate surface.

6. A method for ejecting a cell from within a fluid containing a plurality of cells
to a site on a substrate surface, the method comprising:

(a) positioning a substrate with respect to the cell-containing fluid such that a
25 surface of the substrate faces the surface of the fluid;

(b) identifying a candidate cell in the fluid;

(c) determining the distance between the candidate cell and the fluid surface;
and, providing that the distance determined in (b) is sufficient to enable ejection of the cell
from the fluid onto the substrate surface by application of focused energy,

(d) delivering sufficient focused energy to the fluid to eject the candidate cell therefrom onto a site on the substrate surface, wherein the ejected cell is contained in a droplet of said fluid.

5 7. The method of claim 6, wherein said focused energy comprises focused acoustic energy.

8. The method of claim 6, wherein said focused energy comprises focused electromagnetic energy.

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9. The method of claim 7, wherein steps (b) and/or (c) are carried out by acoustically detecting a localized volume within the fluid that has a different acoustic impedance than said fluid.

15 10. The method of claim 6, wherein step (b) is carried out by identifying the cell as a localized volume having a different refractive index than the fluid.

11. The method of claim 6, wherein step (b) further comprises determining whether the identified candidate cell possesses a particular property, and said delivering of focused acoustic energy in step (d) requires the identified candidate cell to possess said property.

12. The method of claim 6, wherein each of said plurality of cells is substantially the same size and said fluid droplet has a volume that is sufficiently small such that only a single cell can be contained therein.

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13. The method of claim 6, wherein said plurality of cells comprises at least two different groups, with the cells in each group being of substantially the same size and the cells in the different groups differing substantially in mean cell size.

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14. The method of claim 6, wherein the identified candidate cell specifically binds to said site on the substrate surface.

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15. The method of claim 6, wherein steps (a), (b), (c) and (d) are repeated to eject a plurality of candidate cells onto the substrate surface.

16. The method of claim 15, wherein at least a fraction of the candidate cells display a detectable marker molecule.

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17. The method of claim 16, wherein those cells displaying the marker molecule specifically bind to the substrate surface through the marker molecule.

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18. The method of claim 17, further comprising, after each step (d), (e) exposing the substrate to conditions that remove any cell not displaying the marker molecule, thereby providing selective attachment of only those candidate cells displaying the marker molecule.

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19. A method for separating, from a plurality of cells, a cell that displays a marker molecule from a cell not displaying the marker molecule, the method comprising the steps of:

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(a) providing the plurality of cells in a fluid, each cell having an approximately equivalent volume, wherein at least a fraction of the plurality of cells initially present in the fluid display a detectable marker molecule;

(b) positioning a substrate with respect to the cell-containing fluid such that a surface of the substrate faces the surface of the fluid;

(c) identifying a cell in the fluid;

(d) determining the distance between said cell and the fluid surface, and, providing that the distance determined in (c) is sufficient to enable ejection of the cell from the fluid onto the substrate surface by application of focused energy,

(e) delivering sufficient focused acoustic energy to the fluid to eject the cell therefrom onto a site on the substrate surface, wherein the ejected cell is contained in a droplet of said fluid, said droplet having a volume that is sufficiently small so that only a single cell can be contained therein,

(f) repeating steps (a) through (e) to eject a plurality of identified cells onto the substrate surface; and

(g) exposing the substrate surface to conditions that remove any cell not displaying the marker molecule, thereby providing selective attachment of only those candidate cells displaying the marker molecule.

20. The method of claim 19, wherein, if the distance determined in (d) is insufficient to enable ejection of the cell onto the substrate surface, applying focused energy to move the cell closer to the fluid surface.

21. A system for separating, from a plurality of cells, a cell that displays a marker molecule from a cell not displaying the marker molecule, comprising:

(a) a container housing a fluid containing the plurality of cells, each cell having an approximately equivalent volume, wherein at least a fraction of the plurality of cells display a detectable marker molecule;

(b) a substrate positioned with respect to the cell-containing fluid such that a surface of the substrate faces the surface of the fluid, said surface capable of specifically binding the marker molecule to effect specific binding of any cell displaying the marker molecule;

(c) an acoustic ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation generated; and

(d) a means for positioning the ejector in acoustic coupling relationship to the fluid within the container.

22. The system of claim 21, wherein the container further includes an outlet channel that allows the fluid and cells to flow freely out of the container.

5 23. The system of claim 21, wherein at least some of the detectable marker molecules displayed are different.

24. The system of claim 22, wherein the substrate surface comprises a spatial array of localized sites, each localized site capable of specifically binding one of the
10 plurality of different marker molecules.

25. A system for the separation, from a carrier fluid containing a plurality of circumscribed volumes each having a different acoustic impedance than the carrier fluid, of one or more of the circumscribed volumes, the system comprising:

15 a container housing the fluid and having a fluidic channel with an upper opening, said fluidic channel having dimensions permitting the carrier fluid containing said plurality of circumscribed volumes to flow freely through said channel;

 a substrate above said opening having a surface substantially parallel to a plane that contains the opening; and

20 a means for acoustically ejecting from said carrier fluid onto a location on the substrate surface a circumscribed volume having a different acoustic impedance than said carrier fluid.

26. A cellular array comprising a substrate surface on which a plurality of cells
25 is present in an ordered, two-dimensional pattern, with each cell contained within a discrete, substantially planar surface site.

27. A method for screening an ordered, two-dimensional array of individual cells wherein each cell is contained within a discrete, substantially planar surface site, said
30 method comprising delivering a droplet of fluid onto one of said cells, said droplet having

a volume adequate to immerse the cell in the fluid without resulting in the spread of the fluid beyond the site containing the cell.